Tp-e Interval and Tp-e/QT Ratio in Chronic Renal Failure Patients Requiring Hemodialysis

Hemodiyaliz İhtiyacı olan Kronik Renal Yetersizlik Hastalarında Tp-e Aralığı ve Tp-e/QT Oranı

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Özet

Amaç: Kronik renal yetersizlik (KRY) ventriküler aritmi için ana etkenlerden birisidir. Kronik infilamasyon ve diğer faktörler aritmojenik yüzeyin oluşumuna katkıda bulunurlar. Çalışmamızın amacı hemodiyaliz uygulanan KRY hastalarında QT dispersiyonu, hastalarında T dalga zirve ile sonlanım noktası arası mesafe (Tp-e aralığı), Tp-e/QT oranı ve Tp-e/QTc oranını kullanarak ventriküler repolarizasyonu değerlendirmekti. Gereç ve Yöntem: KRY nedeniyle hemodiyaliz tedavisi almakta olan 35 hastanın elektrokardiyogramları incelendi. T dalga zirve ile sonlanım noktası arası mesafe, QT süresi, düzeltilmiş QT süresi ve EKG aralıkları ölçüldü. Yaş ve cinsiyet uyumlu 30 sağlıklı kişinin elektrokardiyogramları ile karşılaştırıldı. Bulgular: KRY grubu ile kontrol grubu birbirlerinden hesaplanmış Tp-e (92.9±24.7 ya karşı 77.0±9.6, p=0.002), Tp-e/QTc (0.20±0.0 a karşı 0.18±0.0, p=0.007) , QTd (58.9±45.6 ya karşı 27.3±7.6, p=0.001) ve Tp-e/QT (0.24±0.1 e karşı 0.21±0.0, p=0.034) açısından anlamlı derecede farklıydı. QTc (457.9±50.8 e karşı 436.4±43.1, p=0.077) ise her iki grupta da benzerdi. Tartışma: QTd, Tp-e, Tp-e/QT ve Tp-e/QTc repolarizasyonu kusurlarını gösteren oldukça yeni göstergelerdir. Bizim bulgularımız bu göstergelerin KRY nedeniyle hemodiyalize giren hastalarda ventriküler elektriksel kararsızlığın belirlenmesinde kullanılabileceğini göstermektedir.

Anahtar Kelimeler

Tp-e; Kronik Renal Yetersizlik; Hemodiyaliz; Aritmi

Abstract

Aim: Chronic renal failure (CRF) is a major factor for ventricular arrhythmia. Chronic inflammation and other factors contribute to formation of arrhythmogenic substrate. The aim of our study was to assess ventricular repolarization in CRF patients receiving hemodialysis, by using QT dispersion, T wave peak to T wave end interval (Tp-e interval), Tp-e/QT ratio, and Tp-e/QTc ratio. Material and Method: Electrocardiogram of 35 CRF patients receiving hemodialysis were studied. T wave peak to end interval, QT and corrected QT intervals and some other ECG intervals were measured. Electrocardiograms of age and sex matched 30 healthy individuals were also analyzed for comparison. Results: CRF group and control group were significantly different from each other for calculated Tp-e (92.9±24.7 vs 77.0±9.6, p=0.002), Tp-e/QTc (0.20±0.0 vs 0.18±0.0, p=0.007) , QTd (58.9±45.6 vs 27.3±7.6, p=0.001), and Tp-e/QT (0.24±0.1 vs 0.21±0.0, p=0.034)values. QTc (457.9±50.8 e karşı 436.4±43.1, p=0.077) values were similar in both groups. Discussion: QTd, Tp-e, Tp-e/QT and Tp-e/QTc are relatively new markers which also indicate repolarization defects. Our findings indicate that these new markers may be useful in determination of ventricular electrical instability in CRF patients receiving hemodialysis.

Keywords

Tp-e; Chronic Renal Failure; Hemodialysis; Arrhythmia

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Introduction

Cardiovascular mortality is high in patients who receive hemodialysis (HD), accounting for 50% of all cause deaths [1]. Cardiac arrhythmias are common in HD patients [2,3]. The reason for increased death and arrhythmias seems multifactorial. Hemodialysis itself predisposes arrhythmias, additional factors such as left ventricle hypertrophy, coronary artery disease, disautonomy and neurohumoral imbalance may contribute in pro-arrhythmic effect [4,5].

For a long time, noninvasive indices of sudden cardiac death derived from surface electrocardiogram (ECG) have been utilized in patients who are at risk of sudden death. These indices mainly depend on the QT interval [6,7]. Prolongation of QT interval, dispersion of QT interval; which is calculated by extracting minimum measured QT interval from maximum measured QT interval, were widely utilized in many studies and were shown to be related with increased sudden death risk in HD patients [8-14].

Recent studies indicate that prolongation of the T wave peak to T wave end interval (Tp-e) on the 12-lead ECG is a marker of ventricular arrhythmogenesis [15-16]. Prolongation of this interval represents a period of potential vulnerability to re-entrant ventricular arrhythmias [17,18]. Prolonged Tp-e has been associated with increased risk of mortality in the congenital and acquired long QT syndromes [19], hypertrophic cardiomyopathy [20] and also in patients undergoing primary PCI for myocardial infarction [21]. However, there is a lack of literature about utilization of Tp-e in HD patients. Aim of our study was to assess ventricular repolarization in patients who receive HD by using QT dispersion, Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio.

Material and Method

Study participants:

Data of whole study group were gained from a retrospective scanning of Bursa Postdoctorate Training and Research Hospital between January 2013 and January 2014. Seventy one patients with CRF receiving hemodialysis were enrolled. Patients with critical coronary stenosis, moderate or severe valvular disease, left and/or right heart failure, atrial fibrillation, right or left bundle block, patients with implanted pacemakers or cardioverter/defibrillators, thyrotoxicosis, diabetes mellitus, and patients under drug treatment that could effect QT interval (e.g. beta blockers, calcium channel blockers, etc) were excluded. Patients who suffer from documented arrhythmogenic diseases such as long QT syndrome, short QT syndrome, Wolff-Parkinson-White Syndrome, Fabry's disease and other storage diseases that affect heart were also excluded. Following exclusion, ECG of consecutive 35 patients receiving HD, were obtained and scanned. All ECGs were performed 30 minutes after HD sessions in these patients. Electrocardiograms of age and sex matched 30 healthy control individuals were also gained from the same institution for comparison.

Measurement of QTd, Tp-e, QT and QRS Intervals from the 12-Lead ECG:

All ECGs were scanned. Electrocardiograms which were faded or showed parasite or atrial/ventricular extra beat on interested leads were excluded. T wave peak to end interval, QT and RR intervals were measured on virtual stage. By using a ruler, Vernier caliper or any other manual measuring tool; getting measurements off from ECG papers could be either inaccurate or slow. Therefore ECG papers were scanned and this made gathering measurements possible in digital environment. These measurements are done by a script which is generated with MATLAB (MathWorks, Natick, Massachusetts, U.S.A.) codes that written by an engineer. The QT interval was defined as extending from the beginning of the QRS complex to where T waves descend onto the isoelectric baseline. When a U wave interrupted the T wave before returning to baseline, the QT interval was measured to the nadir of the curve between the T and U waves. The QTc interval was calculated using the Bazett formula: QTc (ms)=QT measured/√RR (sec). All measurements (Tp-e and other surface ECG related ones) were mean value of three calculations. All measurements were double checked by a blinded engineer. QT dispersion (QTd) was defined as the difference of the highest and the lowest value of the QT interval in the same 12-lead ECG. The Tp-e interval was defined as the interval from the peak of T wave to the end of T wave. Measurements of Tp-e interval were performed from precordial leads as it was described [15].

Statistical Analysis

Statistical analysis was performed using SPSS 13.0 for Windows. Normal distribution of the data was checked using the Kolmogorov–Smirnov test. Continuous variables are presented as means ± standard deviations whereas categorical variables are presented as percentages. The differences between the groups for categorical varieties were compared by the Chi-square test. According to the distribution, the differences between the groups for numeric parameters were compared by Student's t-test or the Mann-Whitney U test. The significance level was assumed as $p < 0.05$.

Results

Data of 65 patients were enrolled for study. Mean age for all group was 46.9±15.5, for HD group 50.3±17.9 and for control group 43.6±10.4 (p=0.066). Hemodialysis group included 60% male patients (n=21) while control group consisted of 40% male patients (n=12, p=0.108). Baseline characteristics and serum electrolytes of both groups were shown in table 1. All biochemical parameters except serum uric acid level were significantly different between both groups.

When it came to comparison of ECG parameters, only QT, QTd, Tp-e, Tp-e/QTc, cQTd, and Tp-e/QT were significantly higher in HD group than controls. Only QTc values were comparable between both groups (Table 2).

Discussion

Because of increased risk of cardiac mortality in this large patient group, risk stratification becomes more and more important to save lives. Newly introduced surface ECG indices may contribute in risk prediction. In this study, significantly prolonged QT, QTd and Tp-e intervals were observed in patients who receive HD than healthy controls. Prolongation of QT interval and increased QT dispersion in end stage renal disease

Table 1.Demographic and clinical characteristics of the compared groups

Parameters	Haemodialysis Patients(n=35)	Controls (n=30)	p value
Age (years)	50.3±17.9	43.6±10.4	0.09
Gender (male%)	60% (21/35)	40% (12/30)	0.08
Systolic blood pressure (mmHg)	128.4±16.5	112±9.2	<0.001
Diastolic blood pressure (mmHg)	76.8±7.5	72.3±7.2	0.017
Body mass index (kg/m2)	27.9±4.4	23.2±5.7	<0.001
Glucose (fasting) (mg/dL)	112.1±62.7	84.7±5.8	<0.001
BUN (mg/dL)	64.5±15.4	29.6±7.0	<0.001
Creatinin (mg/dL)	8.8±0.7	0.7±0.1	<0.001
Na (mg/dL)	139.0±2.6	140.0±2.0	0.017
K (mg/dL)	5.1±0.9	4.2±0.3	<0.001
Uric Acid (mg/dL)	6.2±0.9	6.3±1.1	0.73
Total cholesterol (mg/dl)	201.2±44.0	151.2±34.2	<0.001
Triglyceride (mg/dl)	222.6±83.8	158.4±71.4	<0.001
High density lipoprotein (mg/dl)	32.5±10.4	38.3±8.4	0.018
Low density lipoprotein (mg/dl)	128.4±35.4	85.2±27.0	<0.001
Haemoglobine (mg/dL)	11.2±1.4	13.5±1.5	<0.001
Haematocrite (%)	34.0±4.6	40.0±4.0	<0.001

BUN: Blood urea nitrogen, Na: Sodium; K:Potasium; Data are presented as means ± SD; Data are presented as means ± SD., NS:Nonsignificant

Table 2. Electrocardiographic parameters between the haemodialysis patient with the controls

Parameters	Haemodialysis Patients(n=35)	Controls(n=30)	p value
QT	393.6±55.4	364.0±34.4	0.014
QTc	457.9±50.8	436.4±43.1	0.77
QTd	58.9±45.6	27.3±7.6	<0.001
cQTd	58.6±53.2	31.2±8.2	0.005
Tp-e	92.9±24.7	77.0±9.6	0.002
Tp-e/QT	0.24±0.1	0.21±0.0	0.034
Tp-e/QTc	0.20±0.0	0.18±0.0	0.007

QTc: corrected QT; QTd: QT dispersion; cQTd: corrected QT dispersion TP-e: T wave peak to end interval; Data are presented as means ± SD., NS:Nonsignificant

are subjects of interest for a long time. Previously published articles mainly point out similar findings: these indices of sudden death on the surface ECG are significantly higher in patients receiving HD [6,14]. Hemodialysis itself is pro-arrhythmogenic, but also there is high variety of comorbidities in end stage renal disease patient population. Burden of multiple factors that increase myocardial fibrosis preceding repolarization heterogeneity, electrolyte imbalance that causes myocardium cell depolarization defects, neurohumoral instability with increased automaticity end up with a substrate for sudden cardiac death [4,5]. The mean QTc intervals were similar in our controls and HD patients. The cause of prolonged QT dispersion in HD may be due to regional differences of ventricular wall stress, which may be caused by ventricular dilatation and fibrosis. In addition, transmembrane electrolyte shifts during HD result in an increase in QTc dispersion. Left ventricular hypertrophy and hypertension, well known consequences of the CRF, are also factors relating to prolongation of QT dispersion [22]. It is reported that increasing QTd directly correlates with LVMI of hypertensive patients. Recently, a similar correlation was reported in the HD patients [23]

T wave peak to end interval is a measure of transmural dispersion of repolarization in the left ventricle and accepted as a surrogate for increased ventricular arrhythmogenesis risk. Tp-e/QT and Tp-e/QTc are relatively new markers which also indicate repolarization defects. Published studies clearly suggest the applicability of Tp-e/QT ratio as a potentially important index of arrhythmogenesis, both under the conditions of short, normal and long QT interval, as well as in congenital and acquired channelopathies, in various high-risk populations, such as, patients with long QT syndrome [19], hypertrophic cardiomyopathy [20], post-myocardial infarction [21], inducible ventricular tachycardia [24,25], repaired tetralogy of Fallot [26] or Brugada syndrome [27], Tp-e interval had been found to be more prolonged than control patients.

Underlying mechanism of Tp-e prolongation and ventricular repolarization abnormality was proposed by Antzelevitch and coworkers [18]. As far as authors describe in their numerous articles, there are three identifiable types of cells in ventricle myocardium. One type of these cells is the subendocardial M cell (Mid-myocardial) which has larger late sodium and sodium/calcium exchange currents and a weaker slowly activating delayed rectifier current [28]. The interval of Tp-e corresponds with transmural dispersion of repolarization in the ventricular myocardium, a period during which the epicardium has repolarized and is fully excitable, but the M cells are still in the process of repolarization and vulnerable to the occurrence of early after-depolarization [28]. In suitable conditions, a critical early after-depolarization start a reentry circuit and maintain it for enough time to evolve into polymorphic VT or VF.

As we have mentioned above, Tp-e interval and Tp-e/QT and Tp-e/QTc ratios were validated in various cardiac conditions that may lead to sudden cardiac death. However, there is only one study in the literature that addresses end stage renal disease [29]. In their study, Tun et al. observed that patients receiving HD had significantly longer QT interval, increased QTd and longer Tp-e and longer corrected Tp-e intervals than healthy controls [30]. Results of our study support previous data provided by Tun et al. In addition, we utilized other parameters,Tp-e/QT and Tp-e/QTc, which were recently introduced to literature. While Tp-e/QTc was significantly higher in HD patients, Tp-e/QT showed a tendency of increase without significance. An explanation for this may be the major difference between QT and QTc intervals of HD patients when compared to controls.

In conclusion, our findings indicate that Tp-e, Tp-e/QT and Tp-e/QTc are significantly worse in patients receiving HD than healthy people. These relatively new markers maybe useful in determination of ventricular electrical instability in CRF patients receiving HD. We especially point out that QTc maybe low, and even normal in these patients, an intriguing finding. The limitations of our study include low number of patients and no use of echocardiography in evaluating the patients.

Competing interests

The authors declare that they have no competing interests.

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